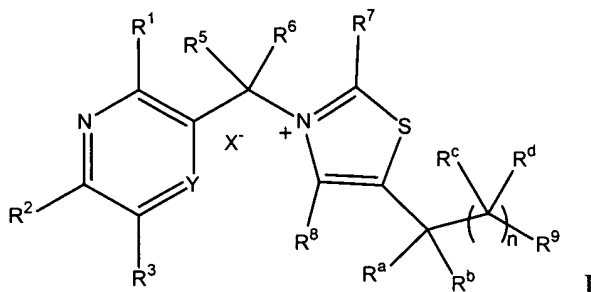


Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Original) A compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

Y is N or C(R⁴);

R¹ is H, alkyl, -N(R)₂, -(CH₂)₁₋₆N(R^o)₂, -(CH₂)₁₋₆OR^o, -NRC(O)R, -C(O)N(R)₂, -CN, -NRSO₂R, -COOR, -OR, -SR, -C(O)R, halo, -OC(O)R, -NRC(O)OR, -OC(O)N(R)₂, -NRC(O)NR, -NRC(S)NR, -NRSO₂NR, -C(O)NRN(R)₂, heteroaryl, or heterocyclyl;

each R², R³ and R⁴ is independently H, alkyl, fluoroalkyl, -C(O)R, -COOR, -C(O)N(R)₂, -CN, -NRC(O)R, -OR, -SR, -N(R)₂, -(CH₂)₁₋₆OR^o, -(CH₂)₁₋₆N(R^o)₂, or halo;

each R⁵ and R⁶ is independently H, alkyl, or fluoroalkyl;

R⁷ is H, alkyl, fluoroalkyl, aralkyl, carbocyclylalkyl, heterocyclyl, carbocyclyl, heterocyclylalkyl, aryl, heteroaryl, heteroaralkyl, -C(O)R, -(CH₂)₁₋₆OR, -(CH₂)₁₋₆N(R)₂, -C(O)CH₂C(O)R, -NRC(O)R, -N(R)₂, -C(O)N(R)₂, or -C(H)(OR)R;

R⁸ is H, alkyl, fluoroalkyl, carbocyclyl, carbocyclylalkyl, heteroaryl, heterocyclyl, -CO₂R, or -CON(R)₂;

R⁹ is -OR¹⁰ or -NR¹¹R¹²;

R¹⁰ is R^o, -C(O)R, -C(O)N(R)₂, -C(O)OR, -(CH₂)₁₋₆-C(O)R, -PO₃M_x, -P(O)(alkyl)OM', -(PO₃)₂M_y, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl, or a tumor-targeting moiety;

x is 1 or 2;

y is 1, 2 or 3;

each M is independently H, Li, Na, K, Mg, Ca, Mn, Co, Ni, Zn, or alkyl;

M' is H, Li, Na, K, or alkyl;

R¹¹ is H or alkyl;

R¹² is H, alkyl, -C(O)R, -C(O)N(R)₂, -C(O)OR, -SO₂R, -SO₂N(R)₂, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl or a tumor targeting moiety;

each R^a and R^b is independently H, OR^o, alkyl, or fluoroalkyl;

each R^c and R^d is independently H, alkyl, or fluoroalkyl;

n is 0-4;

X⁻ is a monovalent or divalent anion, or a counterion to the thiazolium nitrogen located anywhere in the molecule;

R^o is H or alkyl; and

R is R^o, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, or heteroaralkyl;

provided that the following compounds are excluded:

Y is C(R⁴);

R⁵, R⁶, R^a, R^b, R^c and R^d are H;

R⁸ is methyl;

R⁹ is -OR¹⁰, and R¹⁰ is H, -PO₃M_x, -(PO₃)₂M_y or -P(O)(alkyl)OM';

X⁻ is Cl⁻ or Br⁻;

i) R¹ is H, R² is methyl, R³ is -OH, R⁴ is methyl, -CH₂OH or -CH₂NH₂, and R⁷ is H;

ii) R¹ is -NH₂, -NHMe or -N(Me)₂, R² is methyl, R³ is H, R⁴ is H or -CH₃, and R⁷ is H;

iii) R¹ is -NH₂ or OH, R² is methyl, R³ is H, R⁴ is H, and R⁷ is H;

iv) R¹ and R³ are H, R² is methyl, R⁴ is -NH₂, and R⁷ is H;

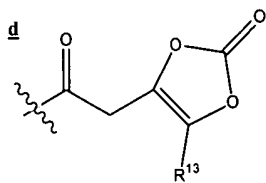
v) R¹ is -NH₂, R² is methyl, R³ and R⁴ are H, and R⁷ is H, -CH(OH)CO₂H or -C(OH)(Me)CO₂H;

vi) R^1 , R^3 , R^4 and R^7 are H and R^2 is methyl; and

vii) R^1 is H, R^2 is $-NH_2$, R^3 is $-OH$, R_4 is $-CH_2CH_2NH_2$, and R^7 is H.

2. (Original) The compound of 1, wherein R^{10} is $-C(O)R$, $-C(O)N(R)_2$, $-C(O)OR$, $-(CH_2)_{1-6}-C(O)R$, alkyl, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclalkyl, aralkyl, heterocyclalkyl, heteroaralkyl, or a tumor-targeting moiety; and R^{12} is $-C(O)R$, $-C(O)N(R)_2$, $-C(O)OR$, $-SO_2R$, $-SO_2N(R)_2$, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclalkyl, aralkyl, heterocyclalkyl, heteroaralkyl or a tumor-targeting moiety.

3. (Original) The compound of 1, wherein R^{10} or R^{12} is a polysaccharide, $-[C(O)CH(R)N(R)]_{2-3}-R$, an antibody, or



, wherein R^{13} is H, alkyl, or aryl.

4. (Canceled)

5. (Currently amended) The compound of [[4]] 1, wherein:

i) R^1 is $-(CH_2)_{1-6}N(R^o)_2$, $-(CH_2)_{1-6}OR^o$, $-NRC(O)R$, $-C(O)N(R)_2$, $-CN$, $-N(R)SO_2R$, $-COOR$, $-SR$, $-C(O)R$, halo, $-OC(O)R$, $-NRC(O)OR$, $-OC(O)N(R)_2$, $-N(R)C(O)N(R)$, $-NRC(S)NR$, $-NRSO_2NR$, $-C(O)NRN(R)_2$, heteroaryl, or heterocyclyl;

ii) R^2 is H, fluoroalkyl, $-C(O)R$, $-COOR$, $-C(O)N(R)_2$, $-CN$, $-NRC(O)R$, $-OR$, $-SR$, $-N(R)_2$, $-(CH_2)_{1-6}OR^o$, $-(CH_2)_{1-6}N(R^o)_2$, or halo;

iii) R^3 is alkyl, fluoroalkyl, $-C(O)R$, $-COOR$, $-C(O)N(R)_2$, $-CN$, $-NRC(O)R$, $-SR$, $-N(R)_2$, $-(CH_2)_{1-6}OR^o$, $-(CH_2)_{1-6}N(R^o)_2$, or halo;

iv) R^4 is fluoroalkyl, $-C(O)R$, $-COOR$, $-C(O)N(R)_2$, $-CN$, $-NRC(O)R$, $-OR$, $-SR$, $-(CH_2)_{1-6}N(R^o)_2$, or halo;

v) R^{10} is H, $-PO_3M_x$, $-(PO_3)_2M_y$ or $-P(O)(alkyl)OM'$; or R^{12} is H or C_{1-6} alkyl; and

vi) n is 1.

6. (Canceled)

7. (Currently amended) The compound of [[6]] 1, wherein:

i) R^1 is H, $-N(R)_2$, alkyl, $-NR^{\circ}C(O)NR$, $-NR^{\circ}C(O)OR$, $-C(O)N(R)_2$, $-(CH_2)_{1-6}N(R^{\circ})_2$, $-NR^{\circ}C(O)R$, $-CN$, $-COOR$, $-OR$, $-SR$, or halo;

ii) R^2 is H, alkyl, fluoroalkyl, $-OR^{\circ}$, $-N(R^{\circ})_2$, or halo;

iii) R^3 and R^4 are independently H, alkyl, $-OR$, $-N(R)_2$, $-(CH_2)_{1-6}OR^{\circ}$, or $-(CH_2)_{1-6}N(R^{\circ})_2$;

iv) R^7 is H, alkyl, fluoroalkyl, $-(CH_2)_{1-6}OR$, $-(CH_2)_{1-6}N(R)_2$, $-NR^{\circ}C(O)R$, $-C(O)R$, $-C(H)(OR)R$, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroaralkyl;

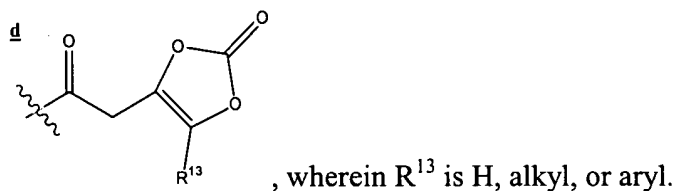
v) R^{10} is H, alkyl, $-C(O)R$, $-PO_3M_x$, $-P(O)(alkyl)OM'$, $-(PO_3)_2M_y$, $-C(O)N(R)_2$, $-C(O)OR$, or a tumor-targeting moiety; or R^{12} is H, alkyl, $-C(O)R$, $-C(O)N(R)_2$, $-C(O)OR$, $-SO_2R$, 5-membered heterocyclyl, 5-membered heteroaralkyl, or a tumor-targeting moiety; and

vi) n is 1.

8. (Currently amended) The compound of [[6 or]] 7, wherein R is R° , carbocyclyl, aryl, heteroaryl, heterocyclyl, aralkyl, heterocyclylalkyl or heteroaralkyl.

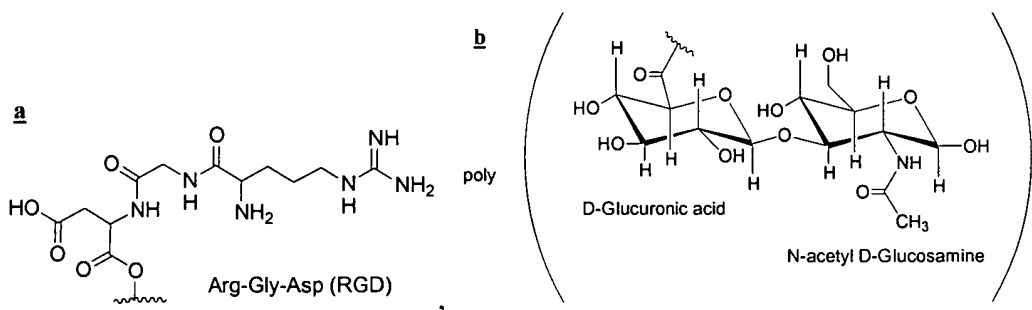
9. (Original) The compound of 8, wherein R° is H or C_{1-6} alkyl optionally substituted with halo, hydroxy or amino.

10. (Currently amended) The compound of [[6 or]] 7, wherein R^{10} or R^{12} is a polysaccharide, $-[C(O)CH(R)N(R)]_{2-3}-R$, an antibody, or

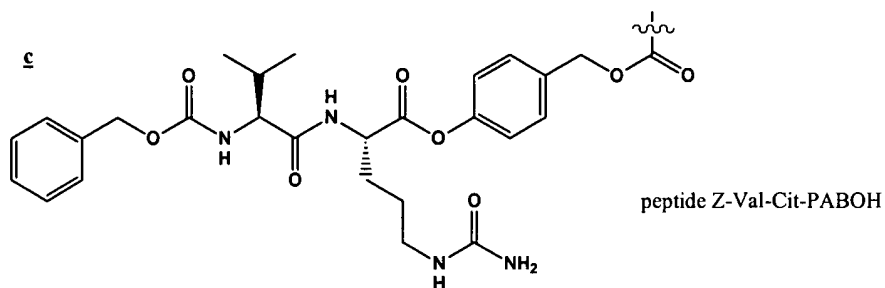


11. (Currently amended) The compound of [[6 or]] 7, wherein said compound has one or more of the features selected from the group consisting of:

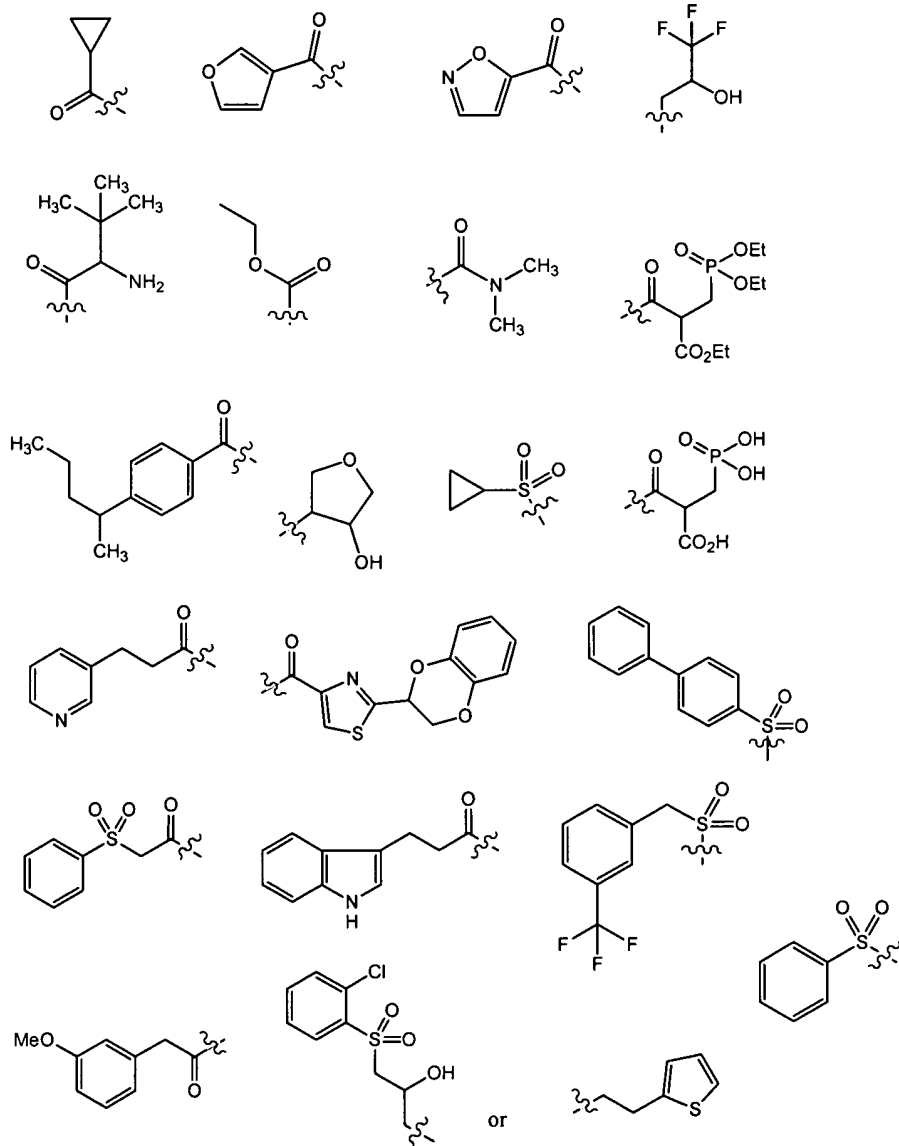
- i) R¹ is H, amino, -CH₂NH₂, -NHC(O)NH₂, -NHC(O)OEt, -NHCH₂OH, -NHCH₂CH₂OH, -NH-CH₂CH₂Cl, -N(CH₂OH)₂, Cl, Br, -SCH₃, CN, -C(O)NH₂, -C(O)OH, methyl, or ethyl;
- ii) R² is H, methyl, ethyl, amino, CF₃, Cl, or Br;
- iii) R³ is H, methyl, ethyl, amino, or hydroxy;
- iv) R⁴ is H, methyl, ethyl, -CH₂OH, or -CH₂NH₂;
- v) each R⁵, R⁶ and R⁸ is independently H, methyl, ethyl, -CH₂F, -CHF₂, or -CF₃;
- vi) R⁷ is H, methyl, ethyl, CF₃, -CH(OH)CH₃, -CH₂OH, or -CH₂CH₂OH; and
- vii) R¹⁰ is H, methyl, ethyl, -C(O)Me, -C(O)Et, -C(O)NMe₂, -C(O)-p-OMe-phenyl, -C(O)O-phenyl, -PO₃H₂, -P(O)(OMe)₂, -P(O)(OMe)OH, -P(O)(Me)OH, -P(O)(OH)OP(O)(OH)(OH), or R¹⁴; and R¹⁴ is selected from the group consisting of:



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Preliminary Amendment



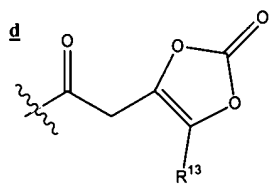
and an antibody; or R^{12} is

H, methyl, ethyl, R¹⁴,

12. (Currently amended) The compound of [[6 or]] 7, wherein ~~said~~ compound has ~~one or more of the features selected from the group consisting of:~~

- i) R^1 is H, $-N(R^\circ)_2$, $-SR^\circ$, or halo;
- ii) R^2 is H, alkyl, fluoroalkyl, $-N(R^\circ)_2$, or halo;
- iii) R^3 and R^4 are independently H or alkyl;
- iv) R^7 is H or alkyl;
- v) R^8 is H or C_{1-6} unsubstituted alkyl; and
- vi) R^9 is $-OR^{10}$ and R^{10} is H, C_{1-6} unsubstituted alkyl, $-C(O)R$, $-PO_3M_x$, $-P(O)(alkyl)OM'$, $-(PO_3)_2M_y$, $-C(O)OR$, or a tumor-targeting moiety.

13. (Original) The compound of 12, wherein R^{10} is a polysaccharide, $-[C(O)CH(R)N(R)]_{2-3}-R$, an antibody, or



, wherein R^{13} is H, alkyl, or aryl.

14. (Currently amended) The compound of 12, wherein ~~said compound has one or more of the features selected from the group consisting of:~~

- i) R^1 is H, $-NH_2$, $-SCH_3$, or Cl;
- ii) R^2 is H, methyl, $-CF_3$, $-NH_2$, or Cl;
- iii) R^3 , R^4 , R^7 and R^8 are independently H or methyl; and
- iv) R^9 is $-OR^{10}$ and R^{10} is H, H, $-PO_3H_2$, $-P(O)(OMe)_2$, $-P(O)(OMe)OH$, $-P(O)(Me)OH$, $-P(O)(OH)OP(O)(OH)(OH)$, or R^{14} ; and R^{14} is as defined in 11.

15. (Original) The compound of 1, wherein said compound is IIa-1, IIa-2, IIa-3, IIa-4, IIa-5, IIa-6, IIa-7, IIa-8, IIa-9, IIa-10, IIa-11, or IIc-1.

16. (Currently amended) A pharmaceutical composition comprising a compound of [[1-15]] 1 and a pharmaceutically acceptable carrier.

17. (Original) The composition of 16, further comprising at least one chemotherapeutic agent, antiangiogenic agent or agent which modulates signaling associated with hypoxic conditions in a cell.

18. (Currently amended) A method for inhibiting transketolase activity in a biological sample or a patient in need thereof comprising contacting said biological sample with or administering to said patient an effective amount of a compound of [[1-15]] 1.

19. (Currently amended) A method for reducing levels of ribulose/ribose-5-phosphate in a cell comprising administering to the cell an effective amount of a compound of [[1-15]] 1.

20. (Currently amended) A method for inhibiting nucleic acid synthesis in a cell comprising administering to the cell an effective amount of a compound of [[1-15]] 1.

21. (Currently amended) A method for inhibiting cell proliferation comprising administering to the cell an effective amount of a compound of [[1-15]] 1.

22. (Currently amended) A method for increasing apoptosis in a tumor cell comprising administering to the cell an effective amount of a compound of [[1-15]] 1.

23. (Currently amended) A method for reducing tumor growth in a patient comprising administering an effective amount of a compound of [[1-15]] 1 ~~or a composition of 16~~ to the patient in need thereof.

24. (Original) The method of 23, further comprising administering at least one chemotherapeutic agent, antiangiogenic agent or agent which modulates signaling associated with hypoxic conditions in a cell.

25. (Currently amended) The method of 23 [[or 24]], further comprising limiting thiamine concentrations in the patient during the administration step.

26. (Original) The method of 25, wherein the patient is on a reduced thiamine diet during the administration step.

27. (Original) The method of 26, wherein cellular thiamine concentrations are maintained at a level sufficient to avoid toxicity associated with thiamine deficiency.